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MRI - Based Brain Age Prediction Using 3D CNN and XAI

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Abstract: ***Brain age is an important biomarker that quantifies age-related structural changes in the human brain, with the potential for early disease diagnosis and monitoring of healthy aging. However, conven-tional three-dimensional (3D) convolutional neural networks require substantial computational resources to achieve high accuracy. In this study, we propose a computationally efficient deep learning model based on two-dimensional (2D) projections that balances efficiency and accuracy. We integrated eight publicly available datasets comprising 7,649 healthy participants aged 5–89 years, using T1-weighted magnetic resonance imaging. In addition to the gray matter probability maps, we incorporated full-brain structural information and multiple projection statistics. These statistics include the mean, standard deviation, median, and maximum to capture the comprehensive morphological features. The proposed architecture comprises only three convolutional blocks with 414,785 parameters and an 86% reduction compared to the similarly highperformance simple fully convolutional network (SFCN). To mitigate systematic prediction biases, we implemented age-distribution-weighted training. The experimental results indicated that single-plane models achieved a mean absolute error (MAE) of approximately 2.7–2.8 years, whereas a three-plane ensemble reduced the error to 2.50 years. After bias correction, the error was 2.54 years, effectively mitigating age-related bias while maintaining accuracy. However, prediction reliability in the middle-aged subgroup remains limited owing to data scarcity, with MAE reaching 7.48 years in the 40–49 age range. The model outperformed the existing 2D projection methods with extremely low computational complexity, requiring only approximately 1.5 h of training. This training time is nearly two orders of magnitude faster than that of the 3D approaches. Furthermore, gradient-weighted class activation mapping visualizations confirmed biological plausibility, highlighting aging-related regions such as the ventricles, cortex, and hippocampus.***

Index Terms: ***Brain age estimation, convolutional neural networks, deep learning, magnetic resonance imaging, two dimentional projections.***

I. PROBLEM STATEMENT

Brain ageing is a natural biological process that leads to gradual structural and functional changes in the brain over time. These changes include grey matter reduction, cortical thinning, white matter degradation, and ventricular enlargement, which can be observed in structural MRI scans. However, the rate of brain ageing differs among individuals, and some people experience accelerated ageing that may lead to memory loss, reduced decision-making ability, slow cognitive processing, and increased risk of neurological disorders. Detecting such accelerated ageing at an early stage is extremely important for preventive healthcare, yet it remains a significant challenge in medical practice. Currently, brain ageing assessment is largely dependent on manual MRI analysis and cognitive evaluation tests. Manual interpretation requires high expertise, is time consuming, and may vary between radiologists, leading to inconsistency in diagnosis. Cognitive tests, while useful, measure functional decline rather than structural brain changes and may not accurately reflect early neurological alterations. Traditional statistical models such as linear regression and basic machine learning algorithms like Support Vector Machines and Random Forests have been used for brain age estimation, but they often rely on handcrafted features and fail to capture the complex three-dimensional spatial patterns present in MRI data. Although deep learning approaches improve prediction accuracy, many of these models function as black-box systems, providing predicted brain age without explaining the underlying reasons. The lack of transparency reduces trust among medical professionals and limits the clinical adoption of such systems. Furthermore, existing methods typically do not provide risk categorization, human impact analysis, or personalized recommendations, making them less useful for practical decision making. Therefore, there is a clear need for an intelligent, automated, and explainable system that can accurately estimate biological brain age from MRI scans while identifying key ageing aspects, determining risk levels, explaining the causes of ageing, and describing potential real-world human problems. The proposed project aims to address these limitations by developing a 3D CNN-based brain age prediction model integrated with Explainable AI techniques to provide accurate, interpretable, and clinically meaningful results.

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II. INTRODUCTION

Brain age is a neuroimaging-based biomarker that quantifies the structural changes in the human brain associated with chronological aging. T1-weighted structural magnetic resonance imaging (MRI) provides excellent contrast between gray matter (GM) and white matter (WM), enabling accurate depiction of the brain anatomy. Therefore, it has been widely used in brain-age prediction research. demonstrated that even in cognitively unimpaired elderly individuals, significant brain volumetric changes can be observed within a single year; GM volume in the temporal and frontal lobes markedly decreases, whereas the hippocampus and amygdala shrink annually by 0.84% and 0.81%, respectively. WM volume also declines at a rate of approximately 0.58% per year, underscoring the strong association between brain structural changes and age, and providing a biological foundation for brain age prediction models [2], [3], [4], [5], [6], [7]. The accurate characterization of age-related changes is essential for establishing reliable prediction models. Such models can support early disease diagnosis, personalized medical decision-making, and the monitoring of healthy aging.

III. RELATED WORK

A. *Two-Dimensional Projections*

Langner et al. [28] demonstrated that projecting 3D whole body MRI data into 2D images enables the application of CNNs to predict attributes such as chronological age. Building on this idea, Jönemo et al. [25] proposed a 2D projection-based approach for brain age prediction, in which 3D brain volumes were projected onto the coronal, axial, and sagittal planes, and both mean and standard deviation images were generated. This yielded six 2D projections as the CNN inputs. Their method preserved the major structural features while substantially reducing the computational cost, achieving an MAE of approximately 3.40 years. The training efficiency was notably high: only 24 min with early stopping and approximately 3.5 h for all 400 epochs, which is more than two orders of magnitude faster than that of typical 3D CNN methods. However, the accuracy of 2D projection methods still generally lags behind that of 3D CNNs, owing to feature simplification and information loss. In this study, additional projection statistics were introduced, and full-brain information was integrated to reduce the risk of missing crit ical regions and enhance the performance of 2D approaches.

B. *Sex Differences In Brain Aging*

Extensive neuroimaging evidence has confirmed pronounced sex differences in brain aging. On average,the male brain volume is approximately 8– 15% larger than that of females [29], and the patterns of atrophy diverge between sexes. For example, brain weight decreases by approximately 2.7 g per year in males and 2.2 g in females [30]. In a study of 330 elderly individuals aged 66–96 years, Coffey et al. [31] observed substantial increases in cerebrospinal fluid volume in males between ages 65–95 years, whereas females exhibited minimal changes, reflecting more pronounced cortical atrophy in males. Other studies have also reported a faster decline in subcortical structures, such as the thalamus, hippocampus, and amygdala, among males [32], [33], [34]. These findings establish sex as an important moderator of brain aging, and underscore the necessity of incorporating sex information into prediction models. Previous research has shown that late-fusion strategies combining sex and imaging features can improve the predictive accuracy [35], [36], [37].

IV. EXISTING SYSTEM

A. *Manual MRI Analysis*

In traditional clinical practice, brain ageing is assessed by radiologists through detailed visual inspection of MRI scans. Specialists carefully examine structural brain regions such as grey matter, white matter, cortical areas, and ventricles to identify age-related anatomical changes. This evaluation relies on expert knowledge and clinical experience to interpret subtle structural variations observed in imaging.

B. *Cognitive and Neuropsychological Tests*

Brain ageing is also evaluated using standardized cognitive and neuropsychological assessments. These tests measure memory, attention, reasoning ability, problem-solving skills, and decision making capacity. The results help in understanding functional brain performance and identifying possible cognitive decline associated with ageing**.**

C. *Statistical and Rule-Based Methods*

Some existing systems estimate brain ageing using statistical techniques such as Linear Regression, Multiple Regression, and Principal Component Analysis (PCA). These methods analyze selected MRI-derived features, including brain volume, cortical thickness, and regional measurements, to establish relationships between structural changes and chronological age.

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Black-Box Machine Learning Models

Earlier machine learning approaches apply algorithms such as Support Vector Machines (SVM), Random Forest, and Artificial Neural Networks (ANN) to predict brain age from MRI data. These models learn patterns from extracted imaging features and generate age predictions based on trained relationships between MRI characteristics and ageing patterns.

Drawbacks:

- High dependence on expert radiologists.
- Manual MRI analysis is time-consuming.
- Low accuracy for subtle brain changes.
- Inability to handle complex 3D MRI data.
- Black-box predictions without explanation
- No clear risk level assessment.
- Do not explain human problems caused by ageing.
- Lack of personalized recommendations.
- Results vary across different experts.
- Limited support for preventive healthcare.

V. PROPOSED SYSTEM

The proposed system introduces an intelligent brain ageing prediction framework that utilizes structural MRI scans and advanced deep learning techniques to accurately estimate biological brain age. By integrating a 3D Convolutional Neural Network with Explainable AI methods, the system not only predicts brain age but also interprets the underlying structural changes and provides meaningful clinical insights.

A. Brain Age Estimation using 3D CNN (BrainAgeNet Model)

This module employs a 3D Convolutional Neural Network (3D CNN) to process volumetric MRI data and extract complex spatial features related to grey matter, white matter, cortical regions, and ventricular structures.

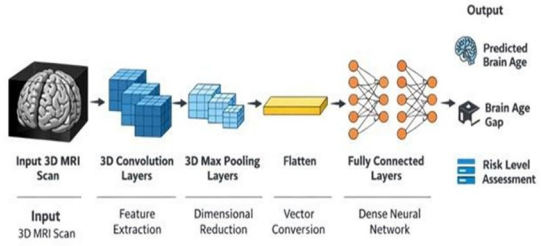


Fig 1

The 3D CNN captures complete three-dimensional anatomical patterns, enabling precise brain age estimation. The trained BrainAgeNet model predicts the biological brain age and computes the brain age gap, which is further used to determine the severity or risk level of brain ageing.

B. Explainable AI-Based Interpretation and Decision Support

To ensure transparency and clinical relevance, the system integrates Explainable AI techniques such as Grad-CAM. This module highlights important brain regions that influence the prediction, allowing users and clinicians to understand the structural basis of accelerated ageing.

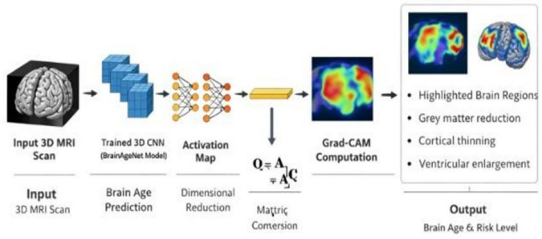


Fig 2

Based on the highlighted regions, the system identifies key ageing aspects, infers possible biological causes, evaluates real-world human impact, and generates personalized recommendations. This approach transforms the prediction model into an interpretable and decisionsupport system for early brain health assessment.

C. *Advantages*

- Enables early identification of accelerated brain ageing.
- Helps people understand their brain health status clearly.
- Provides clear reasons for ageing instead of just numbers.
- Shows real-life problems a person may face due to ageing.
- Supports early preventive action before severe decline.
- Improves clinical decision support for doctors.

VI. FEASIBILITY STUDY

Feasibility analysis evaluates whether the proposed system is practical, implementable, and sustainable. It examines technical, economic, operational, legal, and social aspects to determine the viability of the project.

A. *Technical Feasibility*

The proposed system is technically feasible as it utilizes well-established technologies such as Python, Flask, MySQL, and deep learning frameworks like TensorFlow or PyTorch. The 3D CNN architecture and Explainable AI techniques such as Grad-CAM are widely supported by existing libraries, making development and deployment achievable. Additionally, publicly available MRI datasets provide sufficient data for model training and validation.

B. *Operational Feasibility*

The system is operationally feasible as it is designed with a user-friendly web interface that allows easy MRI upload and result interpretation. Doctors and users can understand the outputs, including risk levels and explanations, without requiring deep technical knowledge. The modular design ensures smooth operation, maintenance, and future scalability of the system.

C. *Economic Feasibility*

The project is economically feasible because it relies primarily on open-source software tools and freely available datasets. There is no requirement for expensive proprietary software. The implementation can be carried out using standard computing resources, making the overall development cost low and suitable for academic and research purposes.

VII. SYSTEM DESIGN

The system architecture follows a modular and layered design that integrates data processing, deep learning, explainable AI, and web-based interaction into a unified framework. The architecture begins with the data layer, where MRI images are uploaded and stored in the database. The preprocessing layer prepares the MRI data through normalization and resizing before passing it to the model layer. The core processing layer consists of a trained 3D Convolutional Neural Network that extracts volumetric brain features and predicts biological brain age. The prediction output is forwarded to the analysis layer, where the brain age gap is calculated and categorized into appropriate risk levels. An interpretation layer applies Explainable AI techniques to highlight important brain regions influencing the prediction. Based on these results, the decision-support layer identifies ageing aspects, infers possible causes, evaluates human impact, and generates recommendations. Finally, the presentation layer displays all outputs, including prediction results, explanations, heatmaps, and reports, through a user-friendly web interface.

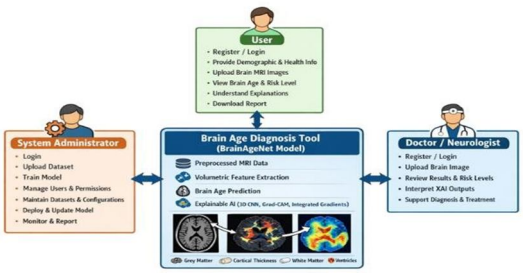


Fig 3

VIII. DATASET DESCRIPTION

The OASIS (Open Access Series of Imaging Studies) dataset is a publicly available neuroimaging dataset that provides high-quality structural brain MRI scans across a broad age range. It is widely used in brain ageing research due to its wellannotated demographic and clinical information. The dataset includes T1-weighted structural MRI images suitable for volumetric analysis and deep learning applications. It covers both healthy individuals and subjects with varying levels of cognitive decline, making it appropriate for studying normal and accelerated brain ageing patterns. The dataset contains cross-sectional as well as longitudinal imaging data, allowing researchers to analyze structural brain changes over time. Each MRI scan is associated with subject-specific metadata such as age, gender, and clinical assessment scores. The data is typically available in standard medical imaging formats such as NIfTI, which can be processed using medical imaging libraries. The wide age distribution supports accurate training of brain age prediction models. It is commonly used for feature extraction involving grey matter, white matter, cortical regions, and ventricular structures. The dataset is freely accessible for academic and research purposes after registration.

A. Relevance to the System

The dataset is highly suitable for training a 3D CNNbased brain age prediction model because it provides volumetric MRI data along with age labels. The age attribute serves as the target variable during model training. Structural features such as grey matter density, cortical thickness, and ventricular size can be learned directly from the MRI scans. The metadata also supports risk analysis and validation of prediction accuracy.

Download Link: https://sites.wustl.edu/oasisbrains/datasets/

IX. MODULES DESCRIPTION

A. Brain Age Diagnosis Tool

The Brain Age Diagnosis Tool functions as the primary application layer of the system, integrating artificial intelligence processing with a web-based user interface. It is developed using Python for backend logic, Flask as the web framework, MySQL for database management, Bootstrap for responsive frontend design, and Wamp Server for local hosting and deployment.

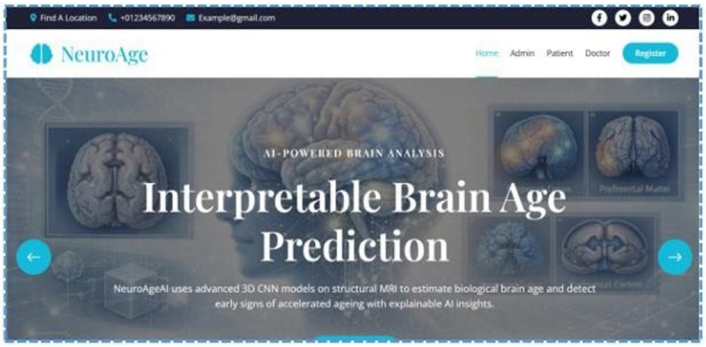


Fig 4

This module acts as the central interface through which all system operations are performed. The tool allows users to upload MRI images, provide demographic information, and initiate brain age analysis. It manages communication between the frontend interface and backend AI modules. Once the MRI is uploaded, the system validates and forwards the data to the trained model for prediction. The tool also handles result visualization, risk categorization, explanation display, and recommendation output. It ensures secure user authentication and structured data storage. Overall, it provides seamless interaction between users and the AI-driven diagnostic system.

B. System User

1) System Admin

The System Admin manages the overall operation of the system, including user access control, dataset organization, and configuration of system parameters. The admin oversees model training, deployment, and updates, while also monitoring system logs, analyzing performance, and generating reports. Additionally, the admin ensures data security, regular backups, and smooth functioning of the server environment.

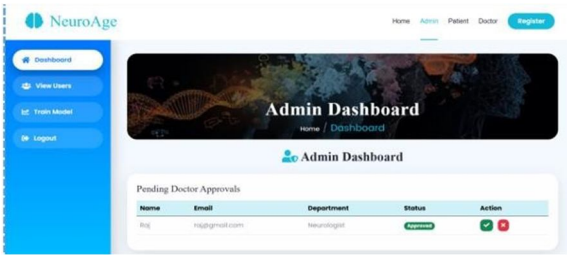


Fig 5

2) User

The User interacts directly with the system for brain ageing assessment. The user uploads MRI images through the web interface and provides personal details such as chronological age. After processing, the user can view the predicted brain age, brain age gap, risk level, explanation, and recommendations. The system presents outputs in a simple and understandable format to ensure usability even for non-technical individuals. The user can access previous reports for comparison and monitoring. This module emphasizes ease of use, clarity of results, and awareness of brain health status.

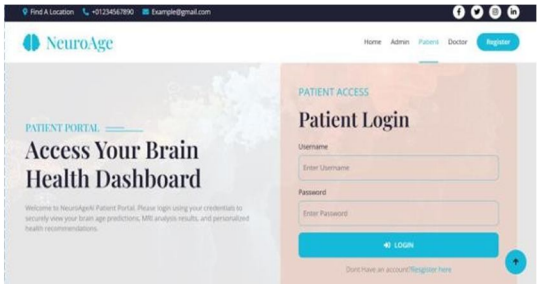


Fig 6

C. BrainAgeNet Model: Build and Train

This module represents the core artificial intelligence component responsible for learning brain ageing patterns from MRI data.

1) Import Dataset

Structural MRI images are imported from a validated dataset and organized systematically. Each record contains MRI data along with subject metadata such as age. The dataset is divided into training, validation, and testing subsets to ensure proper model evaluation. This structured data preparation forms the basis for accurate learning.

2) Pre-processing

Preprocessing ensures that MRI images are standardized before being fed into the deep learning model. The process includes noise reduction, normalization, resizing to uniform dimensions, and conversion into numerical array format. These steps enhance image quality and improve model learning efficiency. Proper preprocessing ensures consistency between training and prediction stages.

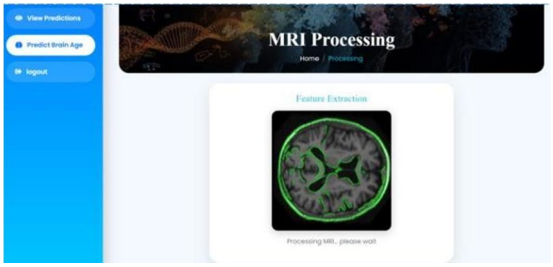


Fig 7

3) Feature Extraction

A 3D Convolutional Neural Network (3D CNN) is used to automatically extract volumetric brain features from MRI scans. Unlike manual feature extraction methods, the 3D CNN learns hierarchical spatial patterns such as grey matter density, cortical structure, and ventricular size.

4) Labelling and Classification

Each MRI image is labeled with its corresponding chronological age. The task is treated as a regression problem where the model learns to predict a continuous numerical value representing brain age. The network minimizes prediction error through loss optimization during training.

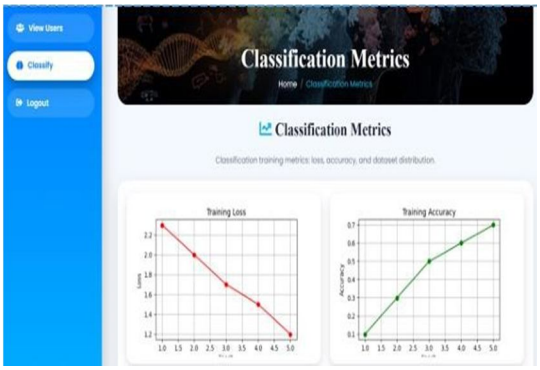


Fig 8

5) Train Model

During training, the Brain Age Net model processes MRI images in batches and updates internal weights using backpropagation. The training process continues until optimal performance is achieved based on validation metrics. This stage enables the model to learn complex spatial relationships associated with brain ageing.

6) Deploy Model

After successful training and validation, the model is deployed within the Flask application. The trained model is saved and loaded dynamically during prediction. This enables real-time brain age estimation when a user uploads a new MRI image.

D. Brain Age Predictor

1) Input MRI Image

In this sub-module, the user uploads a structural brain MRI image through the web interface. The system first validates the uploaded file format and ensures that it meets predefined input specifications.

Once validated, the MRI image undergoes preprocessing steps such as resizing, normalization, and conversion into numerical array format. These preprocessing steps ensure that the input data is consistent with the format used during the model training phase. Proper input handling guarantees that the prediction results remain accurate and reliable.

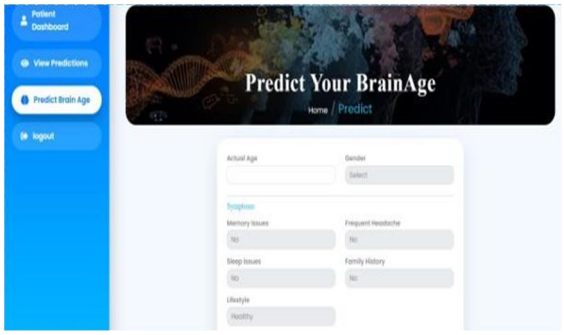


Fig 9

2) Brain Age Prediction

After preprocessing, the MRI image is passed to the deployed BrainAgeNet model. The 3D Convolutional Neural Network analyzes volumetric features such as grey matter distribution, cortical structure, and ventricular size. Based on learned patterns, the model predicts the biological brain age. This predicted age reflects structural brain condition rather than chronological age. The output is a continuous numerical value, which is forwarded to subsequent modules for further analysis.

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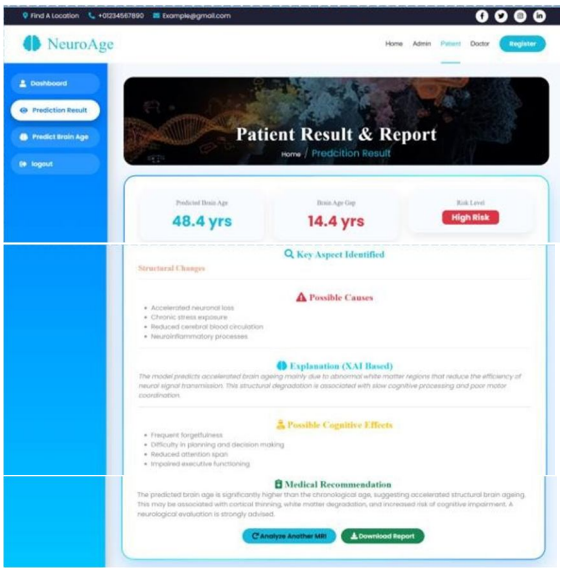


Fig 10

E. Risk Level Assessment

The Risk Level Assessment module evaluates the severity of brain ageing by calculating the brain age gap. The brain age gap is determined by subtracting the user's chronological age from the predicted biological brain age. Based on predefined threshold values, the system categorizes the result into risk levels such as low, moderate, high, or critical. This classification helps users and clinicians quickly understand whether the brain ageing pattern falls within normal range or indicates accelerated ageing. The module ensures that the numerical prediction is translated into a clinically meaningful interpretation. It supports decision-making by clearly identifying the level of concern associated with the ageing condition.

F. AI Interpretation related

The AI Interpretation module integrates Explainable Artificial Intelligence techniques to improve transparency of the deep learning model. Using methods such as Grad-CAM, the system generates visual heatmaps that highlight brain regions contributing most to the prediction. These highlighted areas may include memory-or decisionmaking regions depending on the detected ageing pattern. This module enhances trust and interpretability by visually demonstrating how the model reached its conclusion. It bridges the gap between complex neural network computation and human understanding. By providing region-level explanation, the system becomes more suitable for clinical support and academic research purposes.

G. Recommendation

The Recommendation module provides personalized guidance based on the assessed risk level and inferred causes of ageing. Recommendations may include medical consultation, lifestyle improvements, cognitive training exercises, dietary modifications, and regular monitoring. The system generates suggestions aligned with the severity of detected brain ageing. For low-risk cases, preventive lifestyle advice may be suggested. For higher risk levels, the system may recommend immediate medical evaluation and structured intervention strategies. This module transforms diagnostic results into actionable steps, supporting early intervention and long-term brain health improvement.

H. Reports

The Reports module compiles all analytical results into a structured and comprehensive format. It includes predicted brain age, brain age gap, risk level, ageing causes, AI interpretation highlights, human impact analysis, and personalized recommendations. The report is presented in a user friendly format for viewing and can also be stored in the database for future reference. This module supports longitudinal tracking of brain health by allowing comparison of past and current results. It ensures proper documentation and assists clinicians in reviewing patient history.

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X. CONCLUSION

In conclusion, this project successfully develops an intelligent, MRI-based brain ageing prediction system that combines a 3D Convolutional Neural Network with Explainable AI techniques for accurate and interpretable analysis. The system effectively processes structural brain MRI scans to estimate biological brain age, compute the brain age gap, and classify individuals into meaningful risk levels. The integration of Grad-CAM enhances transparency by highlighting critical brain regions that influence the prediction, improving trust and clinical interpretability. In addition to numerical prediction, the system provides ageing cause inference, human impact assessment, and personalized recommendations, making it a comprehensive decision-support tool rather than a

simple prediction model. Performance evaluation using metrics such as Accuracy, Sensitivity, Specificity, F1-Score, and AUC demonstrates strong classification capability and reliable model generalization. The confusion matrix and ROC analysis further confirm balanced detection of both normal and accelerated brain ageing cases. Thus, the system offers a robust, explainable, and practically applicable framework for early brain health assessment. It supports preventive healthcare strategies, assists clinical decision-making, and contributes to advancements in AI-driven medical imaging research.

XI. FUTURE ENHANCEMENT

A. Integration of Multimodal Brain Imaging

In future work, the system can be extended to incorporate multiple brain imaging modalities such as functional MRI (fMRI) and diffusion-based imaging. Combining structural and functional data would provide a more comprehensive understanding of brain ageing patterns. This enhancement would improve prediction accuracy and enable deeper analysis of neural connectivity and functional decline.

B. Deployment as Cloud-Based Application

The system can be deployed as a secure cloud-based platform, enabling remote access and large scale data analysis. This would allow researchers and healthcare providers to utilize the system globally while maintaining secure data handling practices.

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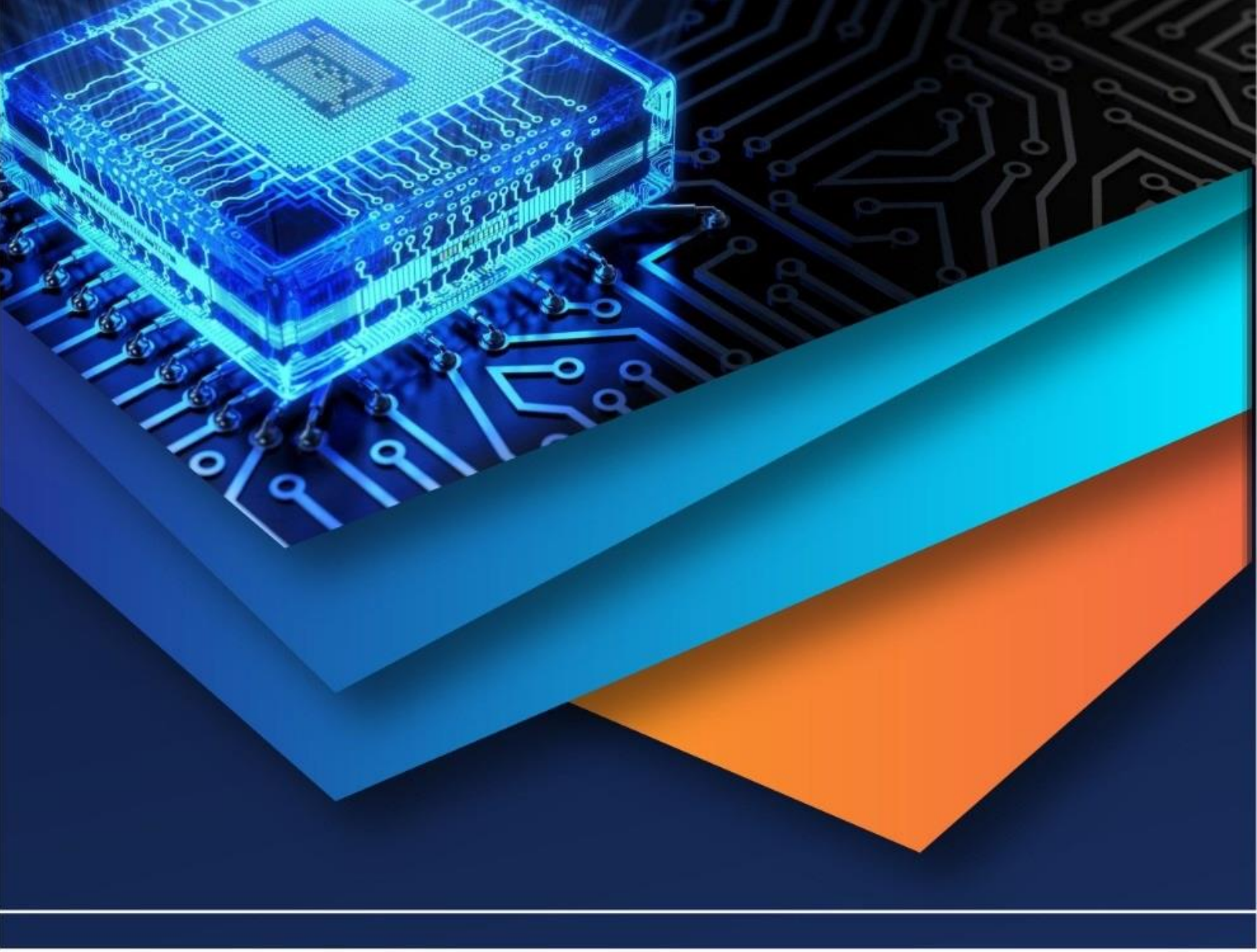


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